

TOPICAL HAZARD EVALUATION PROGRAM OF CANDIDATE INSECT

REPELLENTS AI3-3835..(U) ARMY ENVIRONMENTAL HYGIENE

AGENCY ABERDEEN PROVING GROUND MD J V WADE ET AL. 1983

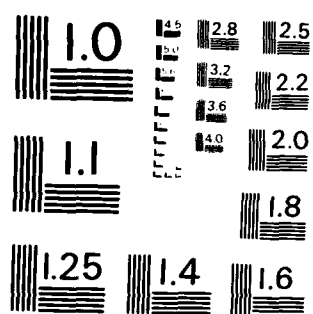
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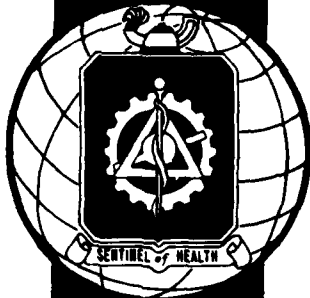
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**UNITED STATES ARMY
ENVIRONMENTAL HYGIENE
AGENCY**

ABERDEEN PROVING GROUND, MD 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF

CANDIDATE INSECT REPELLENTS

AI3-38350a, AI3-38191a, AI3-38195a, and AI3-38196a

US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS

STUDY NOS. 75-51-0328-83 and 75-51-0330-83 thru 75-51-0332-83

JULY 1981 - JANUARY 1983

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REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Chemical AI3-38350a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. Chemicals AI3-38191a, AI3-38195a, and AI3-38196a did not produce skin irritation. Chemical AI3-38350a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. Chemical AI3-38191a produced mild injury to the cornea. Chemicals AI3-38195a and AI3-38196a were noninjurious to the eyes of rabbits. All chemicals tested were relatively nontoxic by ingestion, did not potentiate photo irritation, and did not produce sensitizing reactions.		

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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

CPT Wade/jr/AUTOVON
584-3627

HSRB-OT/WP

16 AUG 1983

SUBJECT: Topical Hazard Evaluation Program of Candidate Insect Repellents
AI3-38350a, AI3-38191a, AI3-38195a, and AI3-38196a, US Department
of Agriculture Proprietary Chemicals, Study Nos. 75-51-0328-83 and
75-51-0330-83 thru 75-51-0332-83, July 1981 - January 1983

Executive Secretary
Armed Forces Pest Management Board
Forest Glen Section, WRAMC
Washington, DC 20307

EXECUTIVE SUMMARY

The purpose, essential findings and recommendations of the inclosed report are as follows:

a. Purpose. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-38350a, AI3-38191a, AI3-38195a, and AI3-38196a by means of laboratory animal studies using Sprague-Dawley rats, New Zealand White rabbits, and albino Hartley guinea pigs.

b. Essential Findings. Chemical AI3-38350a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. Chemicals AI3-38191a, AI3-38195a, and AI3-38196a did not produce skin irritation. Chemical AI3-38350a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. Chemical AI3-38191a produced mild injury to the cornea. Chemicals AI3-38195a and AI3-38196a were noninjurious to the eyes of rabbits. All chemicals tested were relatively nontoxic by ingestion, did not potentiate photoirritation, and did not produce sensitizing reactions.

c. Major Recommendations. Recommend that all chemicals be approved for further testing as candidate insect repellents. If chemicals AI3-38350a or AI3-38191a are accidentally introduced into the eyes, they should be flushed with copious amounts of water.

FOR THE COMMANDER:

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Joel C. Gaydos
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Director, Occupational and
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Dir, Advisory Cen on Tox, NRC
USDA, ARS (Dr. Terrence McGovern)
USDA, ARS-Southern Region (3 cy)
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DEPARTMENT OF THE ARMY
U. S. ARMY ENVIRONMENTAL HYGIENE AGENCY
ABERDEEN PROVING GROUND, MARYLAND 21010

TOPICAL HAZARD EVALUATION PROGRAM
OF
CANDIDATE INSECT REPELLENTS
AI3-38350a, AI3-38191a, AI3-38195a, and AI3-38196a
US DEPARTMENT OF AGRICULTURE PROPRIETARY CHEMICALS
STUDY NOS. 75-51-0328-83 and 75-51-0330-83 thru 75-51-0332-83
JULY 1981 - JANUARY 1983

1. AUTHORITY.

a. Letter, US Department of Agriculture - Agricultural Research, Southern Region, Insects Affecting Man and Animals Research Laboratory, Gainesville, Florida, 18 June 1981.

b. Memorandum of Understanding between the US Army Environmental Hygiene Agency; the US Army Health Services Command; the Department of the Army, Office of The Surgeon General; the Armed Forces Pest Control Board; and the US Department of Agriculture, Agricultural Research, Science and Education Administrations; titled, Coordination of Biological and Toxicological Testing of Pesticides, effective 23 January 1979.

2. REFERENCE. Toxicology Division Standing Operating Procedures, US Army Environmental Hygiene Agency (USAEHA), 1981.

3. PURPOSE. The purpose of this program is to provide guidance for further entomological testing of the candidate insect repellents AI3-38350a, AI3-38191a, AI3-38195a and AI3-38196a, US Department of Agriculture (USDA) Proprietary Chemicals.

4. SUMMARY OF FINDINGS. Hazard evaluations of the candidate insect repellents AI3-38350a, AI3-38191a, AI3-38195a, and AI3-38196a USDA Proprietary Chemicals were conducted by this Agency using New Zealand White rabbits for skin and eye studies, Sprague-Dawley rats for determination of oral toxicity, and albino Hartley guinea pigs for skin sensitivity testing. A tabular presentation of animal toxicity data developed in this Agency follows:*†

* In conducting the studies described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals," US Department of Health, Education and Welfare Publication No. (NIH) 80-23, revised 1978.

† The studies reported herein were performed in animal facilities fully accredited by the American Association for the Accreditation of Laboratory Animal Care.

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Study Nos. 75-51-0328-83 and 75-51-0330-83 thru 75-51-0332-83, Jul 81 -Jan 83

TABLE. PRESENTATION OF DATA

Test	Results	Interpretation
<u>Skin Irritation Studies</u>		
Rabbits		
Single 24-hour application to intact and abraded skin of New Zealand White rabbits.	Chemical AI3-38350a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion.	USAEHA Category II (ref Appendix A)
0.5mL technical grade chemical applied to each of six rabbits.	Chemicals AI3-38191a, AI3-38195a and AI3-38196a did not produce primary irritation of the intact skin and no greater than mild primary irritation of the skin surrounding an abrasion.	USAEHA Category I (ref Appendix A)
<u>Eye Irritation Studies</u>		
Rabbits		
Single 24-hour application of 0.1 mL technical grade chemical to one eye of each of nine New Zealand White rabbits. Three of the nine rabbits had the eye flushed with warm water for 1 minute, 25 seconds after application.	Chemical AI3-38350a produced mild injury to the cornea and, in addition, some injury to the conjunctiva*	USAEHA Category C (ref Appendix A)
	Chemical AI3-38191a produced mild injury to the cornea.*	USAEHA Category B (ref Appendix A)
	Chemicals AI3-38195a and AI3-38196a were noninjurious to the eyes of rabbits.	USAEHA Category A (ref Appendix A)

* Immediate flushing with water reduced injury.

Test	Results	Interpretation
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Approximate Lethal Dose

Oral

Rats (male)-no diluent	AI3-38350a	>4306 mg/kg	These chemicals are relatively nontoxic by ingestion.
	AI3-38191a	>6460 mg/kg	
	AI3-38195a	>6460 mg/kg	
	AI3-38196a	>6460 mg/kg	

Photochemical Skin Irritation Studies

Rabbits

A single 0.05 mL application of a 25% (w/v) solution of each chemical and a 10% (w/v) Oil of Bergamot solution (positive control) in 95% ethyl alcohol were applied to the intact skin of six rabbits. Five minutes after application the rabbits were exposed to ultraviolet (UV) light (365) nm) for 30 minutes at a distance of 10-15 cm.

A 25% solution of each tested chemical in ethanol did not cause a photochemical irritation reaction under test conditions.

All tested chemicals did not cause a photochemical reaction under test conditions and are not expected to cause a photochemical irritation in humans.

Control

Following UV exposures of the rabbits, 0.05 ml of the test chemical, positive control (Oil of Bergamot) and diluent were applied to additional skin areas to serve as unirradiated control sites. Application areas were checked for skin irritation at 24, 48 and 72 hours.

Positive control application and irradiation caused greater irritant effects than in unirradiated skin areas.

Study Nos. 75-51-0328-83 and 75-51-0330-83 thru 75-51-0332-83, Jul 81 -Jan 83

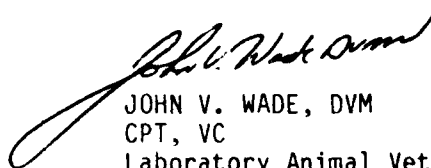
Test	Results	Interpretation
<u>Sensitization Studies</u>		
<u>Guinea Pigs (Male)</u>		
Intradermal (ID) injections of 0.1 mL of a 0.1% solution (w/v) of each tested chemical or of dinitrochlorobenzene (DNCB)* in a mixture containing 1 volume of propylene glycol and 29 volumes of saline.		
Ten test guinea pigs for each chemical were given 10 sensitizing doses over a 3-week period. After a 2-week rest, they were challenged with ID injections of each test compound.	Challenge doses of the tested chemicals did not produce a sensitization reaction.	The tested chemicals did not produce sensitization reactions under test conditions and are not expected to produce sensitization reactions in man.
Ten positive control guinea pigs were sensitized over 3 weeks with DNCB. After a 2-week rest, they were challenged with ID injections of DNCB.	Challenge dose of DNCB in positive control guinea pigs produced a marked sensitization reaction in 10 out of 10 guinea pigs.	The DNCB produced a marked reaction, indicating these guinea pigs respond to sensitizing agents.

* A known skin sensitizer.

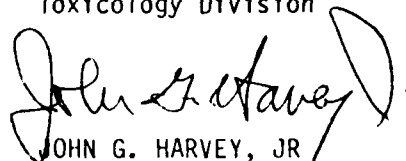
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5. CONCLUSION. Chemical AI3-38350a produced mild primary irritation of the intact skin and of the skin surrounding an abrasion. Chemicals AI3-38195a and AI3-38196a did not produce skin irritation. Chemical AI3-38350a produced mild injury to the cornea and, in addition, some injury to the conjunctiva. Chemical AI3-38191a produced mild injury to the cornea. Chemicals AI3-38195a and AI3-38196a were noninjurious to the eyes of rabbits. All chemicals tested were relatively nontoxic by ingestion, did not potentiate photoirritation, and did not produce sensitizing reactions. These studies were monitored by Analytical Quality Assurance Office (see Appendix B).

6. RECOMMENDATION. Recommend that these USDA Proprietary Chemicals be approved for further testing as candidate insect repellents (under the provisions of the Memorandum of Understanding, para 1b, this report). If chemicals AI3-38350a or AI3-38191a are accidentally introduced into the eyes, they should be flushed with copious amounts of water.



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APPENDIX A

TOPICAL HAZARD EVALUATION PROGRAM
DEFINITIONS OF CATEGORIES OF COMPOUNDS BEING
CONSIDERED FOR ACUTE SKIN APPLICATION

CATEGORY I - Compounds producing no primary irritation of the intact skin or no greater than mild primary irritation of the skin surrounding an abrasion. (INTERPRETATION: No restriction for acute application to the human skin.)

CATEGORY II - Compounds producing mild primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should be used only on human skin found by examination to have no abrasions or may be used as a clothing impregnant.)

CATEGORY III - Compounds producing moderate primary irritation of the intact skin and the skin surrounding an abrasion. (INTERPRETATION: Should not be used directly on the skin without a prophetic patch test having been conducted on humans to determine irritation potential to human skin. May be used without patch testing, with extreme caution, as clothing impregnants. Compound should be resubmitted in the form and at the intended use concentration so that its irritation potential can be reexamined using other test techniques on animals.)

CATEGORY IV - Compounds producing moderate to severe primary irritation of the intact skin and of the skin surrounding an abrasion and, in addition, producing necrosis, vesiculation, and/or eschars. (INTERPRETATION: Should be resubmitted for testing in the form and at the intended use concentration. Upon resubmission, its irritation potential will be reexamined using other test techniques on animals, prior to possible prophetic patch testing in humans, at concentrations which have been shown not to produce primary irritation in animals.)

CATEGORY V - Compounds impossible to classify because of staining of the skin or other masking effects owing to physical properties of the compound. (INTERPRETATION: Not suitable for use on humans.)

EYE CATEGORIES:

A. Compounds noninjurious to the eye. INTERPRETATION: Irritation of human eyes is not expected if the compound should accidentally get into the eyes, provided it is washed out as soon as possible.

B. Compounds producing mild injury to the cornea. INTERPRETATION: Should be used with caution around the eyes.

C. Compounds producing mild injury to the cornea, and in addition some injury to the conjunctiva. INTERPRETATION: Should be used with caution around the eyes and mucosa.

D. Compounds producing moderate injury to the cornea. INTERPRETATION: Should be used with extreme caution around the eyes.

E. Compounds producing moderate injury to the cornea, and in addition producing some injury to the conjunctiva. INTERPRETATION: Should be used with extreme caution around the eyes and mucosa.

F. Compounds producing severe injury to the cornea and to the conjunctiva. INTERPRETATION: Should be used with extreme caution. It is recommended that use be restricted to areas other than the face.

APPENDIX B

ANALYTICAL QUALITY ASSURANCE

The Analytical Quality Assurance Office certifies the following with regard to this study:

a. This study was conducted in accordance with:

(1) Standing Operating Procedures developed by the Toxicology Division, USAEHA.

(2) Title 21, Code of Federal Regulations, 1981 rev, Part 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

b. Facilities were inspected during its operational phase to insure compliance with paragraph a above.

c. The information presented in this report accurately reflects the raw data generated during the course of conducting the study.



PAUL V. SNEERINGER, Ph.D.
Chief, Analytical Quality
Assurance Office

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